APPARATUS FOR FORMING A BIODEGRADABLE IMPLANT PRECURSOR

CROSS-REFERENCE TO RELATED APPLICATIONS

This patent application is a divisional of U.S. patent application Ser. No. 08/127,642, filed Sep. 28, 1993 (now U.S. Pat. No. 5,487,897), which is a continuation-in-part of U.S. patent application Ser. No. 07/783,512, filed Oct. 28, 1991 (now U.S. Pat. No. 5,324,519), which is a continuation-in-part of U.S. patent application Ser. No. 07/384,416, filed Jul. 24, 1989 (now U.S. Pat. No. 5,077,049).

BACKGROUND OF THE INVENTION

In the course of periodontal disease, infection of gingival tissue by plaque bacteria causes the ligaments attaching the gum and teeth to recede, decalcifies the bony structure holding the teeth roots to the bone, and forms periodontal pockets in the gingival tissue adjacent the teeth. Successful periodontal restoration is known to occur if periodontal ligament cells are allowed to colonize root surfaces preferentially over gingival epithelial cells, gingival fibroblasts or osteoblasts. Surgery alone, however, does not result in restoration of lost periodontium.

In an attempt to promote and achieve periodontal restoration, implant technique have been developed. For example, microporous membranes, such as the Millipore® filter and GORE-TEX® membranes, have been developed for use in periodontal tissue regeneration. Typically, the periodontal flap is cut, and the microporous membrane is surgically inserted to cover the surface of the tooth root and to physically occlude epithelial cells from apically migrating along the root surface.

These membranes have several drawbacks. Besides providing variable results, a second surgical entry is needed to remove the membrane after tissue regeneration has been achieved because the membranes are not biodegradable. There is also a higher incidence of infection in connection with their use.

To preclude surgical removal of an implant, membranes made of bioabsorbable material, such as microfibrillar collagen, polylactic acid, and polygalactin (Vicryl®) mesh have been used. Fitting and positioning these membranes to the implant site is cumbersome and time-consuming, and the therapeutic effect of these membranes has been unpredictable. In addition, the degradation time of membranes composed of collagen has been variable, and the risk of adverse immunological reaction to this foreign protein material in the body presents a major concern.

A liquid system containing a biodegradable polymer has been developed wherein the solution is injected into an implant site, and solidifies in situ to form a biodegradable implant having a solid microporous matrix. Advantageously, the implant does not require surgical removal. However, controlled delivery and containment of a liquid system within a particular area within the implant site is difficult, and the liquid may spread to areas other than the implant site.

Therefore, there is a need for an article which will facilitate the controlled placement in an implant site of a liquid polymer solution for forming an implant. A further need is to develop a precursor to a solid implant which is neither all-liquid nor all-solid but will solidify in situ to form a solid microporous implant. There is also a need for a

precursor to a solid implant that can be applied to a tissue defect in an animal and shaped or molded in situ to conform to the defect. Yet another need is to develop in vivo and ex vivo methods of making an implant precursor having such characteristics.

SUMMARY OF THE INVENTION

These and other goals are achieved by the present invention which is directed to an implant precursor for implantation in an animal, such as a human or other mammal, which will eventually harden in situ to a solid implant having a microporous matrix. The invention also provides a method of making and using the implant precursor. An apparatus is also provided for forming an implant precursor ex vivo, and a kit containing the apparatus.

The implant precursor is a two-part structure composed of an outer sac with a liquid content. The implant precursor is composed of a biocompatible, biodegradable and/or bioerodible, water-coagulable thermoplastic polymer or copolymer which is substantially insoluble in an aqueous media, and a pharmaceutically-acceptable, water-soluble organic solvent. The two-part structure of the implant precursor is formed by contacting a portion of a water-coagulable polymer solution with water or other aqueous medium, whereupon the solvent dissipates into the aqueous medium. This causes the polymer on the surface of the portion of polymer solution adjacent the aqueous medium to coagulate to form an outer sac having a firm consistency ranging from gelatinous to waxen-like, while the solution inside the sac (i.e., sac contents) remains a liquid. The sac contents of the implant precursor may range in consistency from watery to slightly viscous.

The implant precursor may be applied to an implant site in an animal, such as a void, a defect, surgical incision, and the like, in or on a hard or soft tissue. Once placed in the implant site, the implant precursor eventually forms a solid microporous implant by the dissipation of the organic solvent into surrounding tissue fluids and the further coagulation of the polymer. Preferably, the matrix of the resulting implant has a two-layered pore structure with a highly porous inner core portion and a comparatively less porous outer surface layer or skin. Pores are formed in the solid matrix of the implant by dissipation of the solvent out of the composition into surrounding tissue fluids. Optionally, the implant precursor may include a separate pore-forming agent that is capable of generating pores within the polymer matrix of the solid implant, as for example, sucrose, sodium chloride, a cellulose-based polymer, and the like.

The resulting solid implant is biodegradable, bioabsorbable, and/or bioerodible, and will be gradually absorbed into the surrounding tissue fluids, as for example, blood serum, lymph, cerebral spinal fluid (CSF), saliva, and the like, and become disintegrated through enzymatic, chemical or cellular hydrolytic action. Generally, the implant will be absorbed over a period of up to about 2 years to about 3 years, preferably within about 1–9 months, preferably within about 60–180 days. The implant may be used, for example, for selective enhancement of cell growth and tissue regeneration, delivery of biologically-active substances to the animal, and the like.

The implant precursor may also include a biologically-active agent, or bioactive agent, as for example, an anti-inflammatory agent, an antiviral agent, an antibacterial or antifungal agent useful for treating and preventing infections in the implant site, a growth factor, a hormone, and the like. The implant resulting from the in situ coagulation of the